

CLAIM AMENDMENTS

1. Cancelled.
2. Cancelled.
3. Cancelled.

4. (Previously Presented) A crystalline form of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ ⁶-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide characterized by the following X-ray diffraction pattern obtained with a Cu $K\alpha$ radiation at 2 θ (2Theta) = 4.5, 6.4, 7.5, 7.7, 8.0, 8.2, 10.0, 10.2, 10.9, 11.1, 12.9, 13.4, 14.0, 14.5, 15.1, 15.6, 16.2, 16.5, 17.3, 17.5, 18.0, 18.9, 19.3, 19.5, 19.9, 20.1, 20.6, 21.0, 21.4, 22.7, 23.1 and 23.6 and an infrared spectrum having sharp bands at 2925, 2854, 1637, 1604, 1484, 1395, 1375, 1285, 1230, 1172, 1125, 1082, 999, 943, 893, 868, 860, 782, 705, 684 cm⁻¹, and wherein the extrapolated melting point (DSC) is 137.2 °C or a pharmaceutically acceptable salt thereof.

5. Cancelled.
6. Cancelled.
7. Cancelled.
8. Cancelled.
9. Cancelled.
10. Cancelled.

11. (Previously Presented) A pharmaceutically acceptable composition comprising the crystalline form of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ ⁶-

thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide characterized by the following X-ray diffraction pattern obtained with a $\text{CuK}\alpha$ radiation at 2θ (2Theta) = 4.5, 6.4, 7.5, 7.7, 8.0, 8.2, 10.0, 10.2, 10.9, 11.1, 12.9, 13.4, 14.0, 14.5, 15.1, 15.6, 16.2, 16.5, 17.3, 17.5, 18.0, 18.9, 19.3, 19.5, 19.9, 20.1, 20.6, 21.0, 21.4, 22.7, 23.1 and 23.6 and an infrared spectrum having sharp bands at 2925, 2854, 1637, 1604, 1484, 1395, 1375, 1285, 1230, 1172, 1125, 1082, 999, 943, 893, 868, 860, 782, 705, 684 cm^{-1} , and wherein the extrapolated melting point (DSC) is 137.2 °C or a pharmaceutically acceptable salt thereof-and a pharmaceutically acceptable carrier.

12. (Previously Presented) A pharmaceutically acceptable composition according to claim 11, wherein the crystalline form of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ^6 -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide is administered as powder in gelatine capsules.

13. Cancelled.
14. Cancelled.
15. Cancelled.
16. Cancelled.
17. Cancelled.
18. Cancelled.
19. Cancelled.
20. Cancelled.
21. Cancelled.
22. Cancelled.
23. Cancelled.

24. Cancelled.

25. Cancelled.

26. Cancelled..

27. Cancelled.

28. (Currently Amended) A process for the manufacture of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ^6 -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide as defined in claim [[1]] 4 comprising

(a) dissolving 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ^6 -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide in 2-propanol under reflux conditions;

(b) subjecting the solution in (a) to polishing filtration;

(c) cooling the solution while stirring over a period of about 6 hours to a temperature of about 10°C;

(d) stirring the slurry at about 10°C until crystals form; and

(e) harvesting the crystals by filtration.

29. (Currently Amended) A process for the manufacture of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ^6 -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide as defined in claim [[1]] 4 comprising

(a) dissolving 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ^6 -thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide in 1-propanol under reflux conditions;

(b) subjecting the solution in (a) to polishing filtration;

- (c) cooling the solution while stirring over a period of about 6 hours to a temperature of about 10°C;
- (d) stirring the slurry at about 10°C until crystals form; and
- (e) harvesting the crystals by filtration.

30. (Previously Presented) The process of claim 28 wherein the 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1 λ ⁶-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide employed in step (a) is prepared by the process comprising

- (a) reacting magnesium, 2-bromo-5-fluorotoluene, and N-tert-butyl-6-chloronicotinamide under reflux to produce N-tert-butyl-6-chloro-4-(4-fluoro-2-methyl-phenyl)-nicotinamide;
- (b) isolating the N-tert-butyl-6-chloro-4-(4-fluoro-2-methyl-phenyl)-nicotinamide;
- (c) reacting N-tert-butyl-6-chloro-4-(4-fluoro-2-methyl-phenyl)-nicotinamide with potassium carbonate and thiomorpholine to produce N-tert-butyl-4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-nicotinamide;
- (d) isolating the N-tert-butyl-4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-nicotinamide;
- (e) adding methanesulfonic acid dropwise to the N-tert-butyl-4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-nicotinamide to produce an emulsion to produce 4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-nicotinamide;
- (f) isolating the 4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-nicotinamide;
- (g) reacting 4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-nicotinamide and potassium hydroxide, methanol, and (diacetoxyiodo)benzene to produce [4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-pyridin-3-yl]-carbamic methyl ester;

- (h) adding a solution of Red-Al dropwise to the [4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-pyridin-3-yl]-carbamic methyl ester to produce methyl-[4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-pyridin-3-yl]-amine;
- (i) adding a solution of 2-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propionyl chloride dropwise into a solution of the methyl-[4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-pyridin-3-yl]-amine to produce 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-[4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-pyridin-3-yl]-isobutyramide; and
- (j) treating the 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-[4-(4-fluoro-2-methyl-phenyl)-6-thiomorpholin-4-yl-pyridin-3-yl]-isobutyramide with oxone at room temperature followed by cooling to about 0°C followed by the dropwise addition of sodium hydrogen sulfite solution to produce 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-[6-(1,1-dioxo-1 λ ⁶-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide.